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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/882,434	06/15/2001	John Michael Manners	CULLN18.1CP1C1	8852

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/882,434	MANNERS ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *3 and 4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5 and 7-22* is/are rejected.

7)☒ Claim(s) *2 and 6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/117,615.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-22 are pending.

2. This application contains claims 3-4 drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. In the response filed 8 December 2003, Applicant again urges that claims 1, 5 and/or 14 are linking claims that that upon their allowance, the restriction should be withdrawn (pg 7-8). This is not found persuasive, for the reasons indicated previously. Claims 1, 5 and/or 14 are not linking claims. There is no consensus sequence that encompasses the wild-type DNA and the mutant DNA. Applicant is reminded that the restriction was made final.

Claim Objections

5. Claims 2, 6-7, 9, 11-13 and 15 are objected to because they have an improper article at the start of the claim.

Claim Rejections - 35 USC § 112

6. Claims 1, 5 and 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 12

March 2003. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that Example 12 details the construction of pPCV91-MiAMP1 from MiAMP1 DNA and plasmid pPCV91, whose source is given in the example; a map of pPCV91-MiAMP1 is shown in Figure 8 (response pg 10).

This is not found persuasive because the source of pPCV91 is a reference, which was not provided. It is not clear if the sequence of that plasmid is known, as it does not appear to be in GenBank. Additionally, the construction process of pPCV91-MiAMP1 requires blunting the vector and the PCR'ed MiAMP DNAs with T4 DNA polymerase. As this process can nibble away at one or more bases beyond the overhang, it is unknown how much nibbling is present in pPCV91-MiAMP1.

Applicant urges that Example 14 details the construction of pET-MiAMP1 from MiAMP1 DNA and plasmid pET-17b, which is commercially available; a map of pET-MiAMP1 is shown in Figure 9 (response pg 10).

This is not found persuasive. The process states that "PCR primer ... engineered to contain restriction sites for NdeI and BamHI" were used to amplify MiAMP1 DNA; the sequences of these primers are not described. Therefore, the construction of pET-MiAMP1 cannot be repeated.

See MPEP 2404.01, which states

> In an application where the invention required access to specific biological material, an applicant could show that the biological material is accessible because it is known and readily available to the public ...
>
> If an applicant has adequately established that a biological material is known and readily available, the Office will accept that showing. In those instances, however, the applicant takes the risk that the material may cease to be known and readily available. Such a defect cannot be cured by reissue after the grant of a patent.
>
> On the other hand, Ex parte Humphreys, 24 USPQ2d 1255 (Bd. Pat. App. & Int. 1992), held that the only manner in which applicants could satisfy their burden of assuring public access to the needed biological material,

and, thereby, compliance with the enablement requirement of 35 U.S.C. 112, was by making an appropriate deposit.

Applicant urges that the specification does describe a repeatable process for preparation of the plasmids, making deposits unnecessary, but asks that is these argument are not persuasive, what additional information would be required for one of ordinary skill in the art to prepare the plasmids (response pg 10).

This is not found persuasive. The specification does not describe a repeatable process for preparation of the plasmid, as discussed above. Applicant must deposit the plasmids.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;
(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

7. Claims 1, 5 and 7-15 remain rejected and claims 16-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a protein comprising amino acids 27-102 of SEQ ID NO:1, constructs comprising the nucleic acids, and cells, plants and reproductive material comprising the constructs, does not reasonably provide enablement for any nucleic acid encoding a protein comprising amino acids 27-102 of

SEQ ID NO:1, encoding a "variant" or "homologue" of that protein, or encoding any *Protoceae* protein that reacts with any antibody to a protein comprising amino acids 27-102 of SEQ ID NO:1, constructs comprising the nucleic acids, and cells, plants and reproductive material comprising the constructs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 12 March 2003, as applied to claims 1, 5 and 7-15. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that the specification defines a homologue as a protein with substantially the same amino acid sequence as that in Figure 6, that the majority of MiAMP1 residues will be present in a homologue at the same relative positions, that cysteine and histidine residues can rarely be substituted, and that homologs include engineered variants in which partial residues have been replaced or that have deletions (response pg 11).

This is not found persuasive. The specification, in the paragraph spanning pg 10-11, states:

> A homologue of the Figure 6 protein is defined as a protein having substantially the same amino acid sequence as the sequence shown in the figure. This means that the majority of residues present in MiAMP1 will be present in a homologue in the same relative position to each other or will be represented by another amino acid residue containing a side chain with similar properties. For example, it is frequently possible to interchange asparagine and aspartic acid; alanine and glycine; serine, threonine and alanine; isoleucine, valine and leucine; as well as lysine and arginine; whereas, cysteine and histidine residues can rarely be substituted with other amino acids (Bordo, D. and Argos, P. 1991 J. Mol. Biol. 217:721-72%. It will be appreciated by one skilled in the art that a homologue may have many conservative substitutions aside from the examples already mentioned. It will also be appreciated by one of skill in the art that homologues include engineered variants of the prototype anti-microbial protein. Such variants may be engineered to provide protein with enhanced activity relative to the prototype protein or altered properties to give a protein with greater utility. It will be further appreciated that homologues include proteins with amino acid deletions at the amino-terminus, the carboxy-terminus, internally, or any combination of the foregoing, provided that the deletion variant has substantially the same anti-microbial activity as the prototype protein.

The definition in the specification means that any amino acid can be substituted or deleted. The majority of residues do not have to be present in a homologue at the same relative positions; amino acids with side chains with "similar" properties can be present instead. "Similar" is not defined. The last paragraph means that any number of deletions can be present, which will affect the "relative positions" of the amino acids, making that phrase meaningless. It is completely unclear from the definition what an engineered variant is and how it differs in sequence from MiAMP1.

Applicant urges that the procedures used to isolate and purify MiAMP1 and test its activity, etc, would be applicable to homologs and variants of MiAMP1, including the hybridization and amplification conditions used to isolate SEQ ID NO:2 (response pg 11-12).

This is not found persuasive. The specification must teach how to make, not how to find. the specification teaches no nucleic acid encoding any "variant" or "homologue" of amino acids 27-102 of SEQ ID NO:1 or encoding any *Protoceae* protein that reacts with any antibody to a protein comprising amino acids 27-102 of SEQ ID NO:1.

Applicant urges, in response to the assertion in the prior Office action that Applicant did not teach the importance of the Greek key ß-barrel, that the specification teaches that substitution of cysteine and histidine should be avoided and that residues in a homologue should be in the same relative positions as in MiAMP1; this would direct one away from destruction of the proteins ability to function as an anti-microbial protein (response pg 12).

This is not found persuasive because the definition quoted above states that cysteine and histidine residues can rarely be substituted, not that they must not be substituted.

Applicant urges that the specification does not teach embarking on making all single amino acid substitutions in MIAMP1 and instead states that residues in a homologue should be in the same relative positions as in MiAMP1 and teaches selective substitution or deletion based on knowledge of what changes would not be expected to destroy anti-bacterial activity (response pg 12).

This is not found persuasive for the reasons above. The specification does not teach changes that would not be expected to destroy anti-bacterial activity.

8. Claims 1, 5 and 7-15 remain rejected and claims 16-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 12 March 2003, as applied to claims 1, 5 and 7-15. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that the invention comprises the identification of a ness class of anti-microbial proteins, with MiAMP1 being the prototype, and have demonstrated in example 10 that homologues of MIAMP1 are abundant in other members of the *Protoceae*; with the information provided one of ordinary skill in the art could isolate and sequences those homologues as a matter of routine (response pg 13).

This is not found persuasive because the instant specification must describe the claimed nucleic acids within the full scope of the claims; the instant specification only describes one nucleic acid.

Applicant urges that *Eli Lilly* and *Amgen* do not apply to the instant case because a prototype molecule has been sequenced at the amino acid and DNA levels; homologues are variants are defined by more than just a name since sequence information, activity and other characteristic can be extrapolated from the prototype (response pg 13).

This is not found persuasive. Genera in the Protoeaceae family include *Adenanthos, Agastachys, Alloxylon, Aulax, Austromuellera, Banksia, Beauprea, Bellendena, Brabejum, Buckinghamia, Cardwellia, Carnarvonia, Cenarrhenes, Conospermum, Diastella, Dryandra, Eidothea, Embothrium, Euplassa, Faurea, Floydia, Franklandia, Gevuina, Grevillea, Hakea, Helicia, Hollandaea, Isopogon, Knightia, Lambertia, Leucadendron, Leucospermum, Lomatia, Macadamia, Mimetes, Musgravea, Neorites, Opisthiolepis, Orites, Orothamnus, Panopsis, Paranomus, Persoonia, Petrophile, Protea, Roupala, Serruria, Sorocephalus, Spatalla, Sphalmium, Stenocarpus, Stirlingia, Symphionema, Synaphea, Telopea, Toronia, Triunia, Vexatorella,* and *Xylomelum.*

Just the *Macadamia* genus includes at least 22 different species, including *M. alticola, M. angustifolia, M. claudiensis, M. erecta, M. francii, M. grandis, M. heyana, M. hildebrandii, M. integrifolia, M. jansenii, M. leptophylla, M. lowii, M. minor, M. neurophyll, M. praealta, M. rousselii, M. ternifolia, M. tetraphylla, M. verticillata, M. vieillardii, M. whelani,* and *M. youngiana.*

The instant specification, however, only describes the structural features of <u>one</u> nucleic acid encoding <u>one</u> anti-microbial protein from <u>one</u> species. The specification fails to describe nucleic acids within the full scope of the claims. *Eli Lilly* and *Amgen* very much apply.

Eli Lilly at pg 1406 states

> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

One is not a representative number of the broadly claimed genus.

Amgen at page 1021 states

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

Applicant only describes the biological property "encoding any *Protoceae* protein that reacts with any antibody to a protein comprising amino acids 27-102 of SEQ ID NO:1" and does not describe any nucleic acid sequence except SEQ ID NO:2.

9. Claims 1-2 and 5-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 12 March 2003. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Claims 1 and 14, part (ii), are indefinite in their recitation of "homologue". The extent to which and nature in which a homologue differs from SEQ ID NO:1 is unclear.

Applicant urges that there is a clear definition in the specification of this term, and thus how a homologue differs from SEQ ID NO:1 is clear (response pg 14).

This is not found persuasive for the reasons discussed in the 112, 1st, rejection above.

Claims 1 and 14, part (iii), are indefinite in their recitation of "variant". The extent to which and nature in which a variant differs from SEQ ID NO:1 is unclear. The extent to which and nature in which a variant differs from a homologue is also unclear.

Applicant urges that here is a clear definition in the specification of this term, and thus how a homologue differs from SEQ ID NO:1 is clear (response pg 14).

This is not found persuasive for the reasons discussed in the 112, 1st, rejection above.

Claims 1 and 14, part (iv), are indefinite in their recitation of "specifically reacts". It is unclear what kind or extent of reaction is specific. It is also unclear how different the activity of the protein can be and still have "essentially the same" anti-microbial activity.

Applicant urges that that an antibody reacts with a high degree of specificity for the antigen to which it has been raised, and the specific reaction between the protein from the *Proteaceae* family and the antibody derives from this specificity (response pg 14).

This is not found persuasive. Does this high specificity mean that the claimed protein is bases 27-102 of SEQ ID NO:1?

Claim Rejections - 35 USC § 102

10. Claims 1, 5, 8-11 and 13-15 rejected under 35 U.S.C. 102(b) as being anticipated by Terras et al (1995, Plant Cell 7:573-588). The rejection is repeated for the reasons of record as set forth in the Office action mailed 12 March 2003. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that specification defines a homologue as a protein with substantially the same amino acid sequence as that in Figure 6, that the majority of MiAMP1 residues will be

present in a homologue at the same relative positions, and that cysteine and histidine residues can rarely be substituted (response pg 15).

This is not found persuasive because, for the reasons detailed in the 112, 1st, rejection above, the definition is meaningless.

Applicant presents a comparison of positions of the cysteine residues in Rs-AFP1 and MiAMP1 to urge that Rs-AFP1 is not a homologue of MiAMP1 as homolog or variant as defined in the specification and thus does not fall within the scope of the claims (response pg 15-16).

This is not found persuasive. The specification does not define homologue or variant in a clear, unambiguous manner, and substitution of cysteines is not excluded.

Claim Rejections - 35 USC § 103

11. Claims 1, 5 and 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terras et al (1995, Plant Cell 7:573-588) in view of Gordon-Kamm et al (1990, Plant Cell 2:603-618). The rejection is repeated for the reasons of record as set forth in the Office action mailed 12 March 2003. Applicant's arguments filed 8 December 2003 have been fully considered but they are not persuasive.

Applicant urges that as discussed above, Terras et al does not anticipate any claim in the instant application and Terras et al in view of Gordon-Kamm et al would not provide any plants transformed with the nucleic acid of the instant claims (response pg 16).

This is not found persuasive. The specification does not define homologue or variant in a clear, unambiguous manner. Thus, Terras et al does anticipate the claims.

12. Claims 2 and 6 would be allowable if rewritten to overcome the objections set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

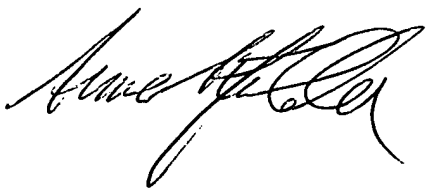
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
February 17, 2004



ANNE KUBELIK
PATENT EXAMINER